

AMENDMENTS TO THE CLAIMS

Claim 1 (currently amended): A ~~non-human~~ transgenic mouse ~~animal~~ whose genome comprises a first nucleotide sequence encoding human CD20 and a second nucleotide sequence encoding a subunit of a heterologous FcγIII receptor, wherein the first nucleotide sequence is operably linked to an endogenous CD20 promoter, and wherein the second nucleotide sequence is operably linked to an endogenous FcγIII receptor promoter.

Claim 2 (currently amended): The transgenic mouse ~~animal~~ of claim 1 wherein said endogenous CD20 promoter is first nucleotide sequence is operably linked to a human endogenous promoter.

Claim 3 (currently amended): The transgenic mouse ~~animal~~ of claim 2 whose cells express human CD20.

Claim 4 (currently amended): The transgenic mouse ~~animal~~ of claim 3 wherein human CD20 is expressed on the surface of B lymphocytes.

Claim 5 (currently amended): The transgenic mouse ~~animal~~ of claim 2, wherein said endogenous FcγIII receptor promoter is second nucleotide sequence is operably linked to a human endogenous promoter.

Claim 6 (currently amended): The transgenic mouse ~~animal~~ of claim 1 wherein said second nucleotide sequence encodes human CD16 alpha chain subtype A.

Claim 7 (currently amended): The transgenic mouse ~~animal~~ of claim 6 wherein said receptor is expressed on the surface of leucocytes.

Claim 8 (currently amended): The transgenic mouse ~~animal~~ of claim 1 ~~7~~ wherein said

receptor is expressed on the surface of one or more cells selected from the group consisting of a cell comprising NK cells, macrophages, neutrophils, eosinophils, basophils, mast cells, and or thymocyte cells ~~or mixtures thereof~~.

Claim 9 (currently amended): The transgenic mouse ~~animal~~ of claim 1 wherein the genome of said mouse ~~animal~~ further comprises a disruption in an endogenous gene encoding a subunit of a receptor substantially homologous to the heterologous Fc γ III receptor.

Claim 10 (currently amended): The transgenic mouse ~~animal~~ of claim 9, wherein the endogenous gene encodes a murine CD16 alpha chain.

Claim 11 (withdrawn—currently amended): A method of identifying an agent capable of treating a B cell lymphoma said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a mouse ~~an animal~~ of claim 1;
- b) administering said agent to the mouse ~~animal~~ of claim 1; and
- c) measuring the level of B lymphocytes expressing human CD20 in the mouse ~~animal~~; wherein a decrease in the number of B lymphocytes expressing human CD20 in the mouse ~~animal~~ after treatment with the agent identifies the agent capable of treating a B cell lymphoma.

Claim 12 (withdrawn): An agent identified according to claim 11.

Claim 13 (withdrawn—currently amended): A method of identifying an agent capable of depleting or killing cells expressing human CD20 said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a mouse ~~an animal~~ of claim 1;
- b) administering said agent to the mouse ~~animal~~ of claim 1; and
- c) measuring the level of B lymphocytes expressing human CD20 in the mouse ~~animal~~;

wherein a decrease in the number of B lymphocytes expressing human CD20 in the mouse ~~animal~~ identifies the agent as capable of depleting or killing cells expressing CD20.

Claim 14 (withdrawn): The method of claim 13 wherein said cells are cancer cells.

Claim 15 (withdrawn): An agent identified according to claim 14.

Claim 16 (currently amended): A cell or tissue derived from the transgenic mouse ~~animal~~ of claim 1.

Claim 17 (cancelled)

Claim 18 (cancelled)

Claim 19 (withdrawn—currently amended): A method of identifying an agent capable of inducing an Fc-mediated effector cell response said method comprising

- a) measuring the baseline level of one or more cytokines associated with an Fc-mediated effector cell response in a transgenic mouse ~~animal~~ of claim 1;
 - b) administering said agent to the transgenic mouse ~~animal~~;
 - c) measuring the level of the cytokines in the mouse ~~animal~~;
- wherein an increase in the level of cytokines after administration identifies the agent as capable of inducing an Fc-mediated effector cell response.

Claim 20 (withdrawn—currently amended): A method of identifying an agent capable of inducing an Fc-mediated effector cell response against B lymphocytes expressing human CD20, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a first transgenic mouse ~~animal~~;

- b) administering said agent to the first transgenic mouse ~~animal~~;
 - c) measuring the level of B lymphocytes expressing human CD20 in the first transgenic mouse ~~animal~~;
 - d) determining the percent reduction in the level of B lymphocytes between step (a) and step (c);
 - e) measuring the level of B lymphocytes expressing human CD20 in a second transgenic mouse ~~animal~~ of claim 1;
 - f) administering said agent to the second transgenic mouse ~~animal~~ of claim 1;
 - g) measuring the level of B lymphocytes expressing human CD20 in the second transgenic mouse ~~animal~~; and
 - h) determining the percent reduction in the level of B lymphocytes between step (e) and step (g);
- wherein if the percent reduction determined in step (h) is greater than the percent reduction determined in step (d), the agent is identified as capable of inducing an Fc-mediated effector cell response against B lymphocytes expressing human CD20.

Claim 21 (withdrawn—currently amended): A method of testing safety of anti- human CD20 therapy, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a mouse ~~an animal~~ of claim 1;
 - b) administering said agent to the mouse ~~animal~~ of claim 1; and
 - c) measuring the level of B lymphocytes expressing human CD20 in the mouse ~~animal~~;
- wherein a decrease in the number of B lymphocytes expressing human CD20 in the mouse ~~animal~~ identifies the agent as capable of depleting or killing cells expressing CD20;
- d) monitoring ~~monitoring~~ the mouse ~~animal~~ for short or long term adverse effects.

Claim 22 (withdrawn—currently amended): A method of testing efficacy of anti- human CD20 therapy, said method comprising:

- a) measuring the level of B lymphocytes expressing human CD20 in a set of mice ~~animals~~ of claim 1;
- b) administering to each mouse ~~animal~~ of the set a different dose of an agent; and
- c) measuring the level of B lymphocytes expressing human CD20 in the mouse ~~animal~~ after each dose; and
- d) determining at least one dose of the agent that results in the most B cell depletion.

Claim 23 (new): The transgenic mouse of claim 1 wherein the first nucleotide sequence is operably linked to a murine endogenous promoter.

Claim 24 (new): The transgenic mouse of claim 1 wherein the second nucleotide sequence is operably linked to a murine endogenous promoter.

Claim 25 (new): The cell or tissue of claim 16 wherein the cell or tissue expresses human CD20.

Claim 26 (new): The cell or tissue of claim 16 wherein the cell or tissue expresses a subunit of human FcγIII receptor.

Claim 27 (new): The transgenic mouse of claim 9 wherein the human CD20 is expressed on the surface of B lymphocytes and human CD16 alpha chain subtype A is expressed on the surface of leucocytes in the transgenic mouse.